

(19) World Intellectual Property Organization  
International Bureau



01 DEC 2004

(43) International Publication Date  
9 October 2003 (09.10.2003)

PCT

(10) International Publication Number  
**WO 03/083037 A2**

- (51) International Patent Classification<sup>7</sup>: **C12M**
- (21) International Application Number: **PCT/US03/09031**
- (22) International Filing Date: **25 March 2003 (25.03.2003)**
- (25) Filing Language: **English**
- (26) Publication Language: **English**
- (30) Priority Data:  
**60/367,876**      **25 March 2002 (25.03.2002)**      **US**
- (63) Related by continuation (CON) or continuation-in-part (CIP) to earlier application:  
**US**      **60/367,876 (CIP)**  
**Filed on**      **25 March 2002 (25.03.2002)**
- (71) Applicant (for all designated States except US): **GEN-ETRONICS, INC.** [US/US]; 11199-A Sorrento Valley Road, San Diego, CA 92064 (US).
- (72) Inventor; and
- (73) Inventor/Applicant (for US only): **RUBUSSAY, Dietmar, P.** [AT/US]; 518 N. Rios Avenue, Solana Beach, CA 92075 (US).
- (74) Agent: **HAILE, Lisa, A.; GRAY CARY WARE & FREIDENRICH LLP**, 4365 Executive Drive, Suite 1100, San Diego, CA 92121-2133 (US).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:**  
— *without international search report and to be republished upon receipt of that report*
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: **MINIMIZING METAL TOXICITY DURING ELECTROPORATION ENHANCED DELIVERY OF POLYNUCLEOTIDES**

(57) Abstract: Methods are provided for introducing a polynucleotide into healthy tissue and generating a pulsed electric field in the tissue via invasive electrodes, resulting in enhanced delivery of the polynucleotide into cells of the tissue, while minimizing local side effects to the electroporated tissue and systemic side effects to the electroporated organism due to metal contaminants released from said electrodes. In one embodiment, the invention methods Use electrodes of gold, gold alloys or other metal that minimize the introduction of toxic amounts of the metal into electroporated tissue. In other embodiments, the invention methods are utilized for the gene therapy by administering DNA to cells of suitable target tissue, and for the induction of an immune response by administration of a DNA vaccine.

WO 03/083037 A2